US Army Medical Research and Materiel

Technology Available for Licensing

Reversed Amidines and Methods of Using for Treating, Preventing, or Inhibiting Leishmaniasis

Features and advantages:

- **Could be used to treat cutaneous, mucocutaneous, or visceral leishmaniasis**
- **Reduces, suppresses, or inhibits *Leishmania* parasites**
- **More effective *in vitro* than pentamidine, the standard treatment**
- **Exhibited good *in vivo* activity against *L. donovani* in a murine model**

Patent Status

Patent No.: 6,706,754 Available from: www.uspto.gov
Issued: March 16, 2004 Docket No.: WRAIR 00-36

Point of Contact

Dr. Paul C. Mele
Director, Office of Research and Technology Applications
USAMRMC, MCMR-ZA-J
504 Scott St., Ft. Detrick, MD 21702-5012
E-mail: usamrmcorta@amedd.army.mil
Voice: 301-619-6664/2065/7219 Fax: 301-619-5034

KEYWORDS: leishmaniasis, chemotherapy, pentamidine

Invention Publication

This invention is a method for preparing and administering one or more reversed amidine compounds for treating, preventing or inhibiting leishmaniasis. Dicationic 2,5-bis (4-guanidinophenyl) furans, 2,5-bis [4-(arylimino) aminophenyl] furans, and 2,5-bis [4-(alkylimino) aminophenyl] furans have been synthesized. These 2,5-bis {[alkyl (or aryl) imino]aminophenyl} furans are referred to as "reversed" amidines as the imino group of the amidine is attached to an "anilino" nitrogen. This is in contrast to the original amidino furans wherein the imino group is directly attached to the aryl ring. The reversed amidines exhibit *in vitro* and *in vivo* activity against *Leishmania* parasites.

Few drugs or compounds exist which exhibit activity against leishmaniasis, of which there are three major clinical variants caused by several different *Leishmania* species. All the variants are spread through the bite of a sandfly. The cutaneous variant can manifest as a single skin ulceration at the bite site soon after it occurs or appear later as disseminated lesions. The mucocutaneous variant begins like the cutaneous variant and then progresses to mouth, nose, or pharynx lesions. The visceral variant involves the reticuloendothelial system.

The reversed amidines exhibited *in vitro* and *in vivo* activity against leishmaniasis that was more effective than [illegible]idine, the standard treatment drug. Pentamidine [illegible] little activity when tested *in vitro* against macrophages infected with *Leishmania*. However, the reversed amidine compounds suppressed or inhibited *L. mexicana* and *L. donovani* infections in the macrophages [illegible] micromolar concentrations. In general, the [illegible]ounds exhibit *in vivo* activity against *L. donovani* in a murine model of visceral disease that is superior to that of pentamidine.

Licensing Opportunities • Patent licenses are available to companies with commercial interests